CLAIMS

1. A tissue engineering scaffold for cell, tissue or organ growth comprising a biocompatible porous polyurethane cellular material comprising a plurality of voids interconnected by pores, the cellular material having a void content from 85% to 98% and a surface area to volume ratio of from 5 to 400 $mm^2/mm^3$.

2. A scaffold as claimed in claim 1 wherein the surface area to volume ratio is from 10 to 200 $mm^2/mm^3$.

3. A scaffold as claimed in the preceding claims wherein the surface area to volume ratio is from 20 to 80 $mm^2/mm^3$.

4. A scaffold as claimed in claim 1 wherein the void mean diameter ranges from 20 to 300 microns.

5. A scaffold as claimed in claim 4 wherein the void mean diameter is from 40 to 250 microns.

6. A scaffold as claimed in claim 5 wherein the void mean diameter is from 80 to 200 microns.

7. A scaffold as claimed in any preceding wherein the voids are substantially spherically shaped.

8. A scaffold as claimed in any preceding claim wherein the pore diameters are 10 to 50% of the void diameters.

9. A scaffold as claimed in any preceding claim wherein the pores are generally elliptically shaped.

10. A scaffold as claimed in any preceding claim wherein the material consists of three-dimensional cells with flattened faces at points of contact therebetween.

11. A scaffold as claimed in claim 10 wherein any given cell has up to 14 faces.

12. A scaffold as claimed in claim 11 wherein some of the faces contain interconnecting pores between adjacent cells.

13. A scaffold as claimed in any of claims 4 to 12, wherein the average number of interconnecting pores in any given cell is from 2 to 14.

14. A scaffold as claimed in claim 13 wherein the average number of interconnecting pores in any given cell is from 1 to 7.

15. A scaffold as claimed in any preceding claim wherein less than 10% of the voids have less than 2 pores.

16. A scaffold as claimed in any preceding claim wherein the cellular material is cleaned using a solvent with a solubility parameter of from 17MPa$^{0.5}$ to 27 MPa$^{0.5}$.

17. A scaffold as claimed in any preceding claim wherein the cellular material has a soft phase and hard phase .

18. A scaffold as claimed in claim 17 wherein the polar ratio of the polymer is from 1.4:1 to 10:1.

19. A scaffold as claimed in claim 18 wherein the polar ratio of the polymer is from 2:1 to 5:1.

20. A scaffold as claimed in claim 17 wherein the cellular material has a hard segment context of from 35 to 65%.

21. A scaffold as claimed in claim 20 wherein the cellular material has a hard segment context of from 35 to 55%.

22. A scaffold as claimed in claim 21 wherein the cellular material has a hard segment context of from 40 to 50%.

23. A scaffold as claimed in any preceding claim where the cohesive energy density of the hard phase is at least $2MPa^{1/2}$ greater than the cohesive energy density of the soft phase.

24. A scaffold as claimed in any preceding claim wherein the leachables content of the cellular material is less than 1.0mg per gram when extracted in water.

25. A scaffold as claimed in any preceding claim wherein the leachables content of the cellular material is less than 10μg per gram when extracted in water.

26. A scaffold as claimed in any preceding claim wherein the leachables content of the cellular material is less than 0.1μg per gram when extracted in water.

27. A scaffold as claimed in any preceding claim wherein the scaffold is manufactured from

diphenyl methane diisocyanate (MDI) with a 2,4 MDI isomer content of less than 3%;

a linear, long chain diol which is free of tertiary carbon linkages;

water;

a cross-linking agent;

a trimerisation catalyst;

a blowing and/or gelling catalyst; and

a surfactant.

28. A scaffold as claimed in claim 27 wherein the diol is polytetramethylene ether glycol (PTMEG).

29. A scaffold as claimed in claim 27 wherein the diol is a polycarbonate diol.

30. A scaffold as claimed in claim 29 wherein the polycarbonate diol is a reaction product of one or more diols with a carbonate monomer.

31. A scaffold as claimed in any of claims 27 to 30 wherein the diol molecular weight is between 400 and 5000.

32. A scaffold as claimed in claim 31 wherein the diol molecular weight is between 500 and 2500.

33. A scaffold as claimed in any of claims 27 to 32 wherein the trimerisation catalyst is a carboxylate.

34. A scaffold as claimed in claim 33 wherein the trimerisation catalyst is a potassium acetate.

35. A scaffold as claimed in claim 34 wherein potassium acetate is present in the reaction formulation in an amount of from 0.02% to 0.12% by mass of the formulation.

36. A scaffold as claimed in any of claims 27 to 35 wherein the cross-linking agent is present in the reaction formulation in an amount of from 1% to 5% by mass.

37. A scaffold as claimed in claim 36 wherein the cross-linking agent is trialkanol amine.

38. A scaffold as claimed in claim 37 wherein the cross-linking agent is triethanolamine.

39. A scaffold as claimed in any preceding claim wherein the isocyanate index of the reaction formulation is from 1.03 to 1.20.

40. A scaffold as claimed in claim 39 wherein the index is approximately 1.13.

41. A scaffold as claimed in any of claims 27 to 40 wherein the reaction formulation includes a chain extender.

42. A scaffold as claimed in claim 41 wherein the chain extender is a linear aliphatic diol.

43. A scaffold as claimed in claim 42 wherein the linear aliphatic diol is 1, 4 butane diol.

44. A scaffold as claimed in any of claims 41 to 43 wherein the chain extender is present in the formulation in an amount of less than 7% by mass.

45. A scaffold as claimed in claim 44 wherein the chain extender is present in the formulation in an amount of less than 4% by mass.

46. A scaffold as claimed in any of claims 27 to 45 wherein water is present in the reaction formulation in an amount of from 0.6% to 1.8% by mass.

47. A formulation for forming a tissue engineering scaffold according to any preceding claim comprising: -

an isocyanate;

a chain extender;

water; and

a cross linking agent,

wherein the isocyanate is MDI with a 4,4 MDI isomer content of greater than 97% and wherein the isocyanate index of the reaction formulation is from 1.03 to 1.20.

48. A formulation as claimed in claim 47 wherein the isocyanate index is approximately 1.13.

49. A formulation for forming a tissue engineering scaffold of any of claims 1 to 46 comprising:

diphenyl methane diisocyanate (MDI) with a 2,4 MDI isomer content of less than 3%;

a linear, long chain diol which is free of tertiary carbon linkages;

water;

a cross-linking agent;

a trimerisation catalyst;

a blowing and/or gelling catalyst; and

a surfactant.

50. A formulation as claimed in claim 49 wherein the diol is polytetramethylene ether glycol (PTMEG).

51. A formulation as claimed in claim 49 wherein the diol is a polycarbonate diol.

52. A formulation as claimed in claim 51 wherein the polycarbonate diol is a reaction product of one or more diols with a carbonate monomer.

53. A formulation as claimed in any of claims 49 to 52 wherein the diol molecular weight is between 400 and 5000.

54. A formulation as claimed in claim 53 wherein the diol molecular weight is between 500 and 2500.

55. A formulation as claimed in any of claims 49 to 54 wherein the trimerisation catalyst is a carboxylate.

56. A formulation as claimed in claim 55 wherein the trimerisation catalyst is a potassium acetate.

57. A formulation as claimed in claim 56 wherein potassium acetate is present in the reaction formulation in an amount of from 0.02% to 0.12% by mass of the formulation.

58. A formulation as claimed in any of claims 49 to 57 wherein the cross-linking agent is present in the reaction formulation in an amount of from 1% to 5% by mass.

59. A formulation as claimed in claim 58 wherein the cross-linking agent is trialkanol amine.

60. A formulation as claimed in claim 59 wherein the cross-linking agent is triethanolamine.

61. A formulation as claimed in any of claims 49 to 60 wherein the isocyanate index of the reaction formulation is from 1.03 to 1.20.

62. A formulation as claimed in claim 61 wherein the index is approximately 1.13.

63. A formulation as claimed in any of claims 49 to 62 wherein the reaction formulation includes a chain extender.

64. A formulation as claimed in claim 63 wherein the chain extender is a linear aliphatic diol.

65. A formulation as claimed in claim 64 wherein the linear aliphatic diol is 1, 4 butane diol.

66. A formulation as claimed in any of claims 63 to 65 wherein the chain extender is present in the formulation in an amount of less than 7% by mass.

67. A formulation as claimed in claim 66 wherein the chain extender is present in the formulation in an amount of less than 4% by mass.

68. A formulation as claimed in any of claims 49 to 67 wherein water is present in the reaction formulation in an amount of from 0.6% to 1.8% by mass.

69. A process for preparing a tissue engineering scaffold as claimed in any of claims 1 to 46 comprising the steps of:-

preparing a isocyanate terminated prepolymer in an excess of isocyanate;

preparing a polyol reaction mixture comprising a polyol, a chain extender, a catalyst, a blowing agent, a cross linking agent, a catalyst and a surfactant;

mixing the prepolymer and the polyol

dispensing the mixed reaction ingredients into a mould;

post curing the reaction ingredients; and

solvent extracting the material with a solvent having a solubility parameter of from 17 to 27 $MPa^{0.5}$.

70. A process as claimed in claim 69 including the step, prior to solvent extraction, of crushing the moulded cellular material thus formed to increase the open cell content of the material.

71. A process as claimed in claims 69 or 70 wherein the prepolymer is prepared from a prepolymer reaction mixture at a temperature of from 70 to 80°C.

72. A process as claimed in any of claims 69 to 71 wherein the prepolymer reaction mixture is reacted for a period of from 1 to 2 hours.

73. A process as claimed in any of claims 69 to 72 wherein the prepolymer reaction mixture is stirred continuously under a dry inert atmosphere.

74. A process as claimed in any of claims 69 to 73 wherein the rotational mixing element for mixing the prepolymer reaction mixture is configured to generate turbulent mixing.

75. A process as claimed in any of claims 69 to 74 wherein during moulding the mould temperature is maintained at not less than 30°C.

76. A process as claimed in claim 75 wherein the mould temperature is from 50 to 80°C.

77. A process as claimed in any of claims 69 to 76 including the step of venting the mould during moulding to facilitate free rise.

78. A process as claimed in any of claims 69 to 77 wherein the volume of the mould is such as to facilitate at least a ten fold volumetric expansion of the reaction ingredients.

79. A process as claimed in any of claims 69 to 78 wherein the volume of the mould is such as to facilitate a less than 50 fold volumetric expansion of the reaction ingredients.

80. A process as claimed in any of claims 69 to 79 wherein the post curing is carried out at a temperature of at least 20°C for a period of at least 30 minutes.

81. A process as claimed in claim 80 wherein the post-curing is carried out at a temperature of approximately 80°C.

82. A process as claimed in claim 80 or 81 wherein the post-curing is carried out in a post-cure oven.

83. A process as claimed in any of claims 69 to 82 wherein the post-curing is carried out in a $CO_2$ rich environment.

84. A process as claimed in any of claims 69 to 83 wherein the moulded cellular material is crushed by greater than 80% of the pre-crushed volume of the material.

85. A process as claimed in any of claims 69 to 84 wherein the crushing is carried out in the presence of a solvent.

86. A process as claimed in any of claims 69 to 85 wherein the extraction solvent used for solvent extraction has a polar component of its solubility parameter in excess of $3MPa^{0.5}$.

87. A process as claimed in any of claims 69 to 86 wherein the solubility parameter of the extraction solvent is within $\pm 4$ $Mpa^{0.5}$ of the solubility parameter of the polymeric material or its phases.

88. A process as claimed in any of claims 69 to 87 wherein the vapour pressure of the extraction solvent is greater than 2 kPa at 25°C.

89. A process as claimed in claim 88 wherein the vapour pressure of the extraction solvent is greater than 5 kPa at 25°C.

90. A process as claimed in claim 89 wherein the vapour pressure of the extraction solvent is greater than 10 kPa at 25°C.

91. A process as claimed in any of claims 69 to 90 wherein the extraction solvent has a solubility parameter of from 18 to 24 $MPa^{0.5}$.

92. A process as claimed in any of claims 69 to 91 wherein the extraction solvent used for solvent extraction is water miscible.

93. A process as claimed in any of claims 69 to 92 wherein the extraction solvent used for solvent extraction is a swelling solvent.

94. A process as claimed in 93 wherein the swelling solvent swells the material by more than 30%.

95. A process as claimed in claim 94 wherein the swelling solvent swells the material by more than 100%.

96. A process as claimed in claim 94 or 95 wherein the swelling solvent swells the material by more than 150%.

97. A process as claimed in any of claims 69 to 95 wherein the extraction solvent used for solvent extraction includes tetrahydrofuran (THF).

98. A process as claimed in any of claims 69 to 97 wherein the extraction solvent used for solvent extraction includes methyl ethyl ketone (MEK).

99. A process as claimed in any of claims 69 to 98 wherein the solvent extraction step is carried out for a period of at least 2 hours at room temperature.

100. A process as claimed in any claims 69 to 99 including the step of de-swelling the solvent swollen polymeric material.

101. A process as claimed in claim 100 wherein the polymeric material is de-swelled by contacting the solvent swollen polymeric material with a non-solvent which is miscible with the extraction solvent.

102. A process as claimed in any of claims 69 to 101 including the step of drying the polymeric material to substantially remove solvent residues.

103. A process as claimed in claim 102 including the step, prior to drying, of extracting the polymeric material with water.

104. A process as claimed in any of claims 69 to 103 wherein the polymeric material is extracted with a number of extraction solvents.

105. A process as claimed in claim 104 wherein the solvent extractions are carried out sequentially.

106. A process as claimed in any of claims 101 to 105 wherein the non solvent is an alcohol.

107. A process as claimed in any of claims 101 to 106 wherein the non solvent is added to the solvent swollen polymeric material in an amount and at a rate to maintain a low concentration gradient.

108. A process as claimed in any of claims 101 to 107 wherein the de-swelling is carried out at a temperature of less than 40°C.